

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT ✓
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

Figure 1 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
8	5'-CCTACTAG <u>C</u> GTTCATC-3' (133-1)
9	5'-CCTACTAGCXTTCATC-3' (139-2)
10	5'-CCTACTAXCGTTCTCATC-3' (133-2)
11	5'-CCTACTXGCGTTCTCATC-3' (139-3)
12	5'-CCTACXAGCGTTCTCATC-3' (133-3)
13	5'-CCTAXTAGCGTTCTCATC-3' (139-4)
14	5'-CCTXCTAGCGTTCTCATC-3' (133-4)
15	5'-CCTXCTAG <u>C</u> TTCTCATC-3' (145-10a)
16	5'-CCTACTAGCGXTCTCATC-3' (133-5)
17	5'-CCTACTAGCGTXCTCATC-3' (139-7)
18	5'-CCTACTAGCGTTXTCATC-3' (133-6)
19	5'-CCTACTAGCGTTCXCATC-3' (139-8)
20	5'-CCTXXTAGCGTTCTCATC-3' (133-12)
21	5'-XXTAGCGTTCTCATC-3' (139-6)
22	5'-CCTACTAGCGTTCXXATC-3' (139-9)
23	5'-CCTXCTXGCGTTCTCATC-3' (145-10b)

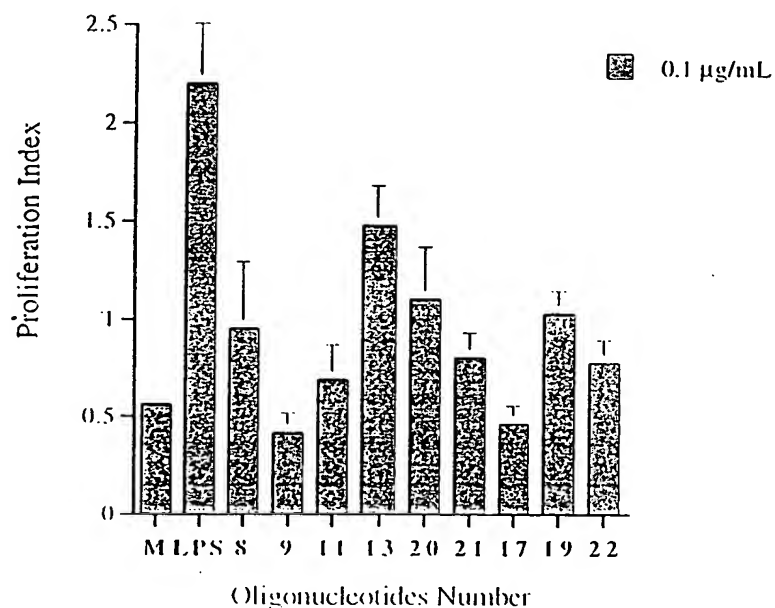
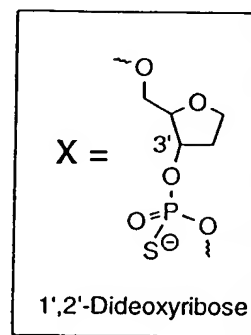


Figure 2 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
8	5'-CCTACTAG <u>CG</u> TTCTCATC-3' (133-1)
9	5'-CCTACTAGCXTTCTCATC-3' (139-2)
10	5'-CCTACTAXCGTTCTCATC-3' (133-2)
11	5'-CCTACTXGCGTTCTCATC-3' (139-3)
12	5'-CCTACXAGCGTTCTCATC-3' (133-3)
13	5'-CCTAXTAGCGTTCTCATC-3' (139-4)
14	5'-CCTXCTAGCGTTCTCATC-3' (133-4)
15	5'-CCTXCTAG <u>CG</u> TTCTCATC-3' (145-10a)
16	5'-CCTACTAGCGXTCTCATC-3' (133-5)
17	5'-CCTACTAGCGTXCTCATC-3' (139-7)
18	5'-CCTACTAGCGTTXTCATC-3' (133-6)
19	5'-CCTACTAGCGTTCXCATC-3' (139-8)
20	5'-CCTXXTAGCGTTCTCATC-3' (133-12)
21	5'-XXTAGCGTTCTCATC-3' (139-6)
22	5'-CCTACTAGCGTTCXXATC-3' (139-9)
23	5'-CCTXCTXGCGTTCTCATC-3' (145-10b)

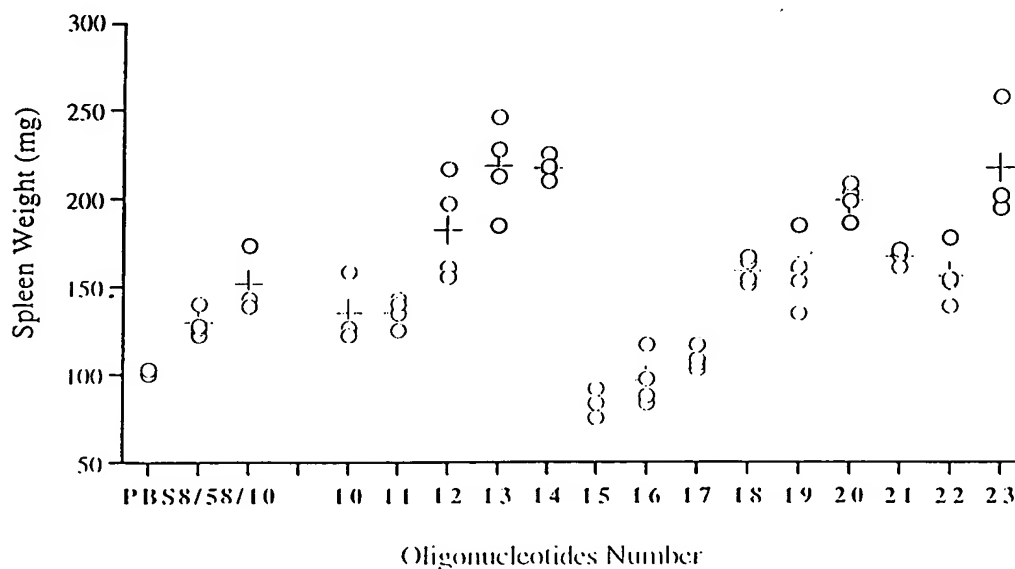
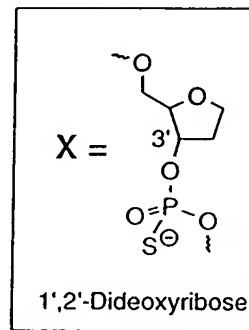


Figure 3 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTCTCTGT-3' (131-1)
2	5'-CTATCTGAXGTTCTCTGT-3' (131-13)
3	5'-CTATCTGXCGTTCTCTGT-3' (131-2)
4	5'-CTATCXGACGTTCTCTGT-3' (131-3)
5	5'-CTAXCTGACGTTCTCTGT-3' (131-4)
6	5'-CTATCTGACGXTCTCTGT-3' (131-5)
7	5'-CTATCTGACGTTXTCTGT-3' (131-6)

$X =$

1',2'-Dideoxyribose

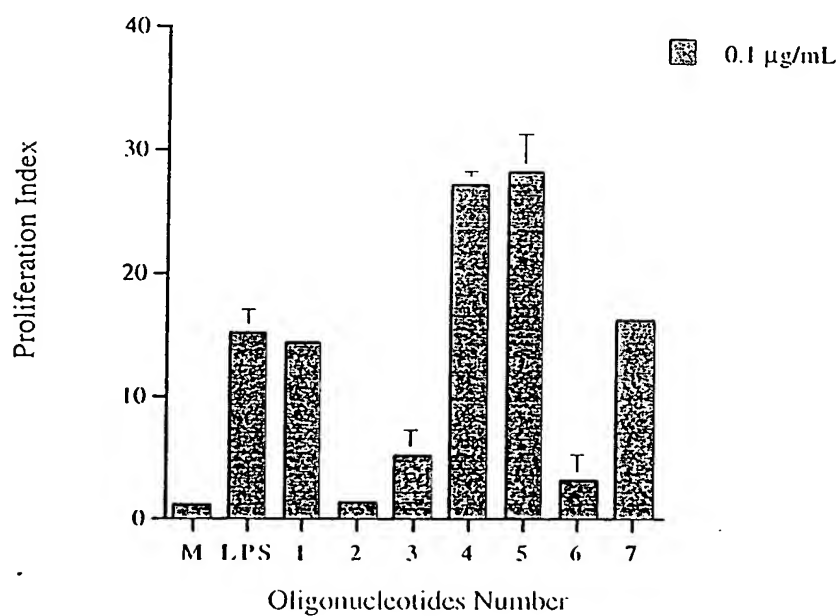


Figure 4 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTCTCTGT-3' (131-1)
2	5'-CTATCTGAXGTTCTCTGT-3' (131-13)
3	5'-CTATCTGXCGTTCTCTGT-3' (131-2)
4	5'-CTATCXGACGTTCTCTGT-3' (131-3)
5	5'-CTAXCTGACGTTCTCTGT-3' (131-4)
6	5'-CTATCTGACGXCTCTGT-3' (131-5)
7	5'-CTATCTGACGTTXTCTGT-3' (131-6)

X =

1',2'-Dideoxyribose

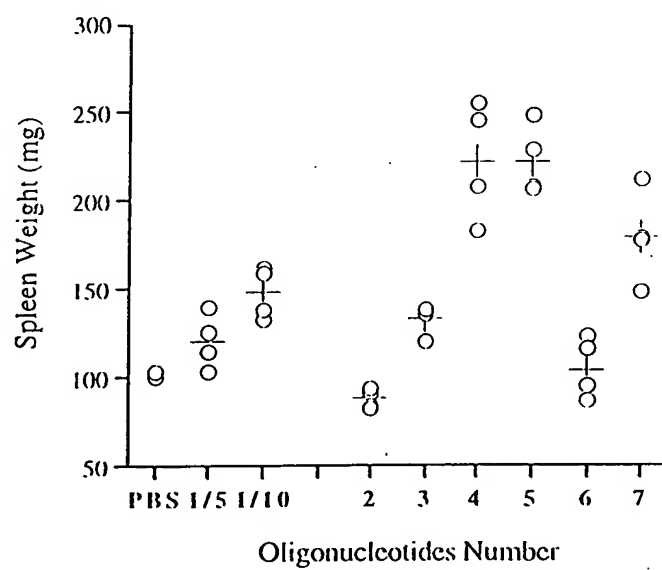


Figure 5 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
133-1	5'-CCTACTAGCGTTCTCATC-3'
141-2	5'-CCTACTAGCXTTCTCATC-3'
141-3	5'-CCTACTXGCGTTCTCATC-3'
141-4	5'-CCTAXTAGCGTTCTCATC-3'
141-5	5'-CCTXXTAGCGTTCTCATC-3'
141-6	5'-XXTACTAGCGTTCTCATC-3'
141-7	5'-CCTACTAGCGTXCTCATC-3'
141-8	5'-CCTACTAGCGTTCXCATC-3'
141-9	5'-CCTACTAGCGTTCXXATC-3'
131-1	5'-CTATCTGACGTTCTCTGT-3'
137-2	5'-CTATCTGXCGTTCTCTGT-3'
137-3	5'-CTATCXGACGTTCTCTGT-3'
137-4	5'-CTAXCTGACGTTCTCTGT-3'

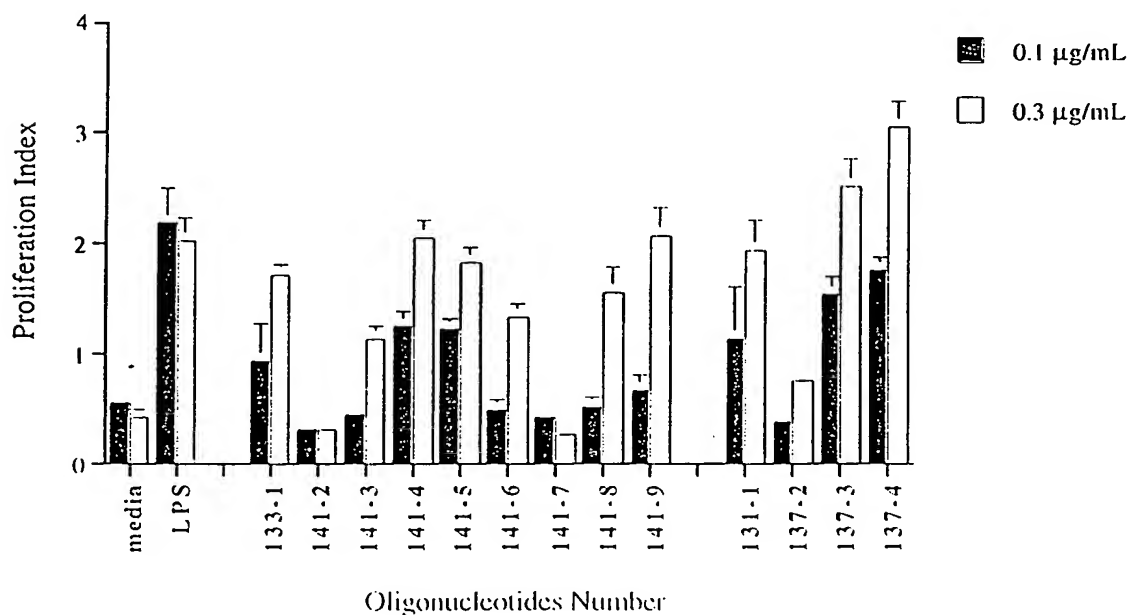
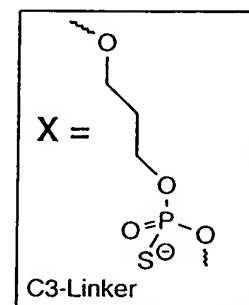
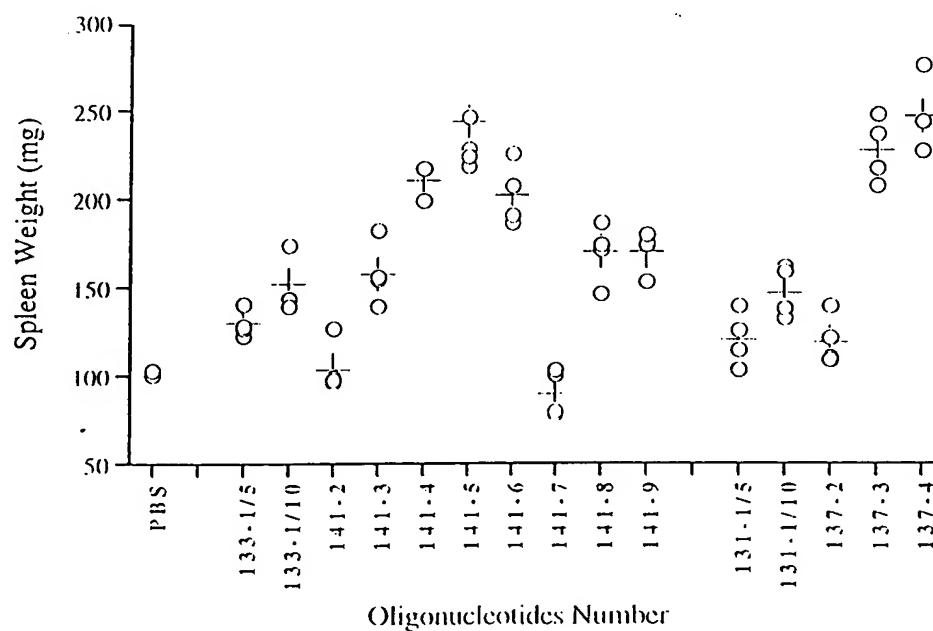
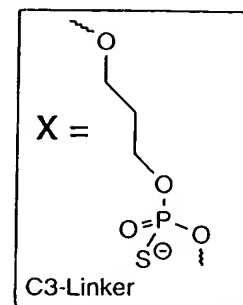
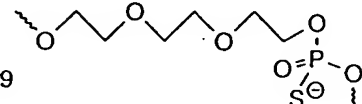


Figure 6 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

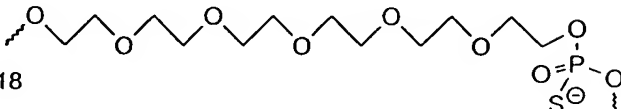
Oligo No.	Sequence & Modification
133-1	5'-CCTACTAGCGTTCTCATC-3'
141-2	5'-CCTACTAGCXTTCTCATC-3'
141-3	5'-CCTACTXGCGTTCTCATC-3'
141-4	5'-CCTAXTAGCGTTCTCATC-3'
141-5	5'-CCTXXTAGCGTTCTCATC-3'
141-6	5'-XXTACTAGCGTTCTCATC-3'
141-7	5'-CCTACTAGCGTXCTCATC-3'
141-8	5'-CCTACTAGCGTTCXCATC-3'
141-9	5'-CCTACTAGCGTTCXXATC-3'
131-1	5'-CTATCTGACGTTCTCTGT-3'
137-2	5'-CTATCTGXCGTTCTCTGT-3'
137-3	5'-CTATCXGACGTTCTCTGT-3'
137-4	5'-CTAXCTGACGTTCTCTGT-3'



Oligo No.	Sequence & Modification
1	5'-CTATCTGACGTTCTCTGT-3' (131-1)
2	5'-CTAXCTGACGTTCTCTGT-3' (153-1)
3	5'-CTATCTGACGTTCTCTGT-3' (153-2)
4	5'-CTAYCTGACGTTCTCTGT-3' (153-3)
5	5'-CTATCTGACGTTCTCTGT-3' (153-4)
6	5'-CCTACTAGCGTTCTCATC-3' (133-1)
7	5'-CCTXCTAGCGTTCTCATC-3' (155-1)
8	5'-CCTACTAGCGTTCTCATC-3' (155-2)
9	5'-CCTYCTAGCGTTCTCATC-3' (155-3)
10	5'-CCTACTAGCGTTCTCATC-3' (155-4)

**X =** 

Spacer9

**Y =** 

Spacer18

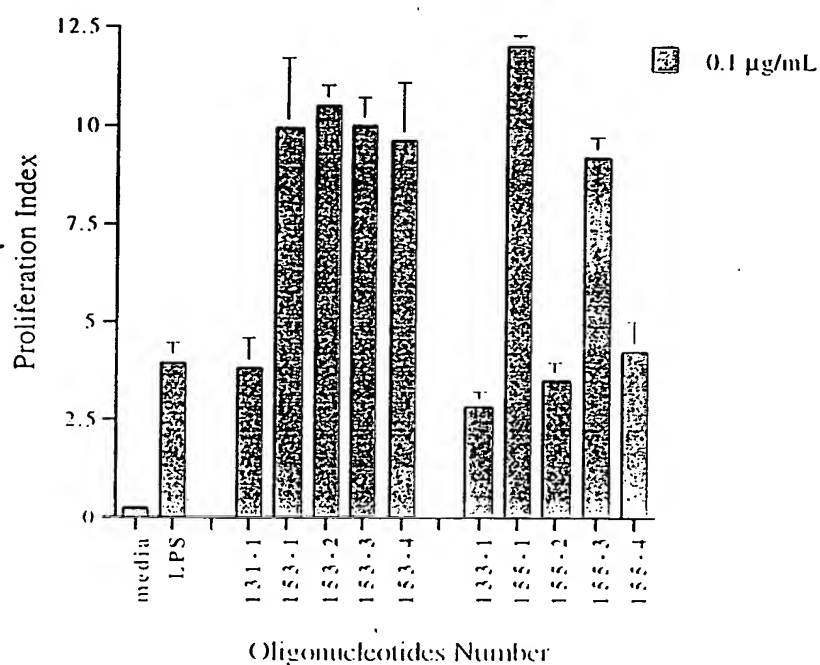




Figure 8 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTCTCTGT-3' (131-1)
2	5'-CTAXCTGACGTTCTCTGT-3' (153-1)
3	5'-CTATCTGACGTT <u>C</u> XCTGT-3' (153-2)
4	5'-CTAYCTGACGTTCTCTGT-3' (153-3)
5	5'-CTATCTGACGTT <u>C</u> YCTGT-3' (153-4)
6	5'-CCTACTAGCGTTCTCATC-3' (133-1)
7	5'-CCTXCTAGCGTTCTCATC-3' (155-1)
8	5'-CCTACTAGCGTT <u>C</u> XCATC-3' (155-2)
9	5'-CCTYCTAGCGTTCTCATC-3' (155-3)
10	5'-CCTACTAGCGTT <u>C</u> YCATC-3' (155-4)

$X =$ 
  
Spacer9

$Y =$ 
  
Spacer18

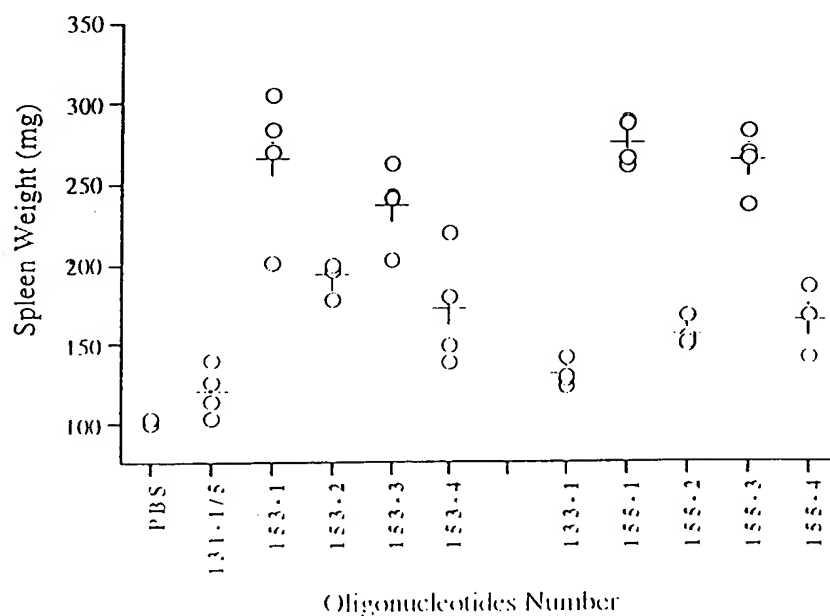
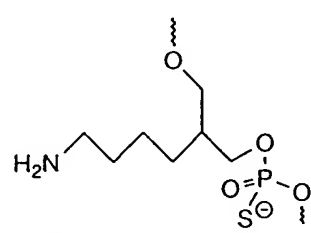


Figure 9 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGACGTTCTCTGT-3' (131-1)
2	5'-CTATCTGXCGTTCTCTGT-3' (157-1)
3	5'-CTATCTXACGTTCTCTGT-3' (157-2)
4	5'-CTAXCTGACGTTCTCTGT-3' (157-3)
5	5'-CTATCTGACGTXCTCTGT-3' (157-4)
6	5'-CTATCTGACGTTCTXCTGT-3' (157-5)

**X =**



Amino-Linker

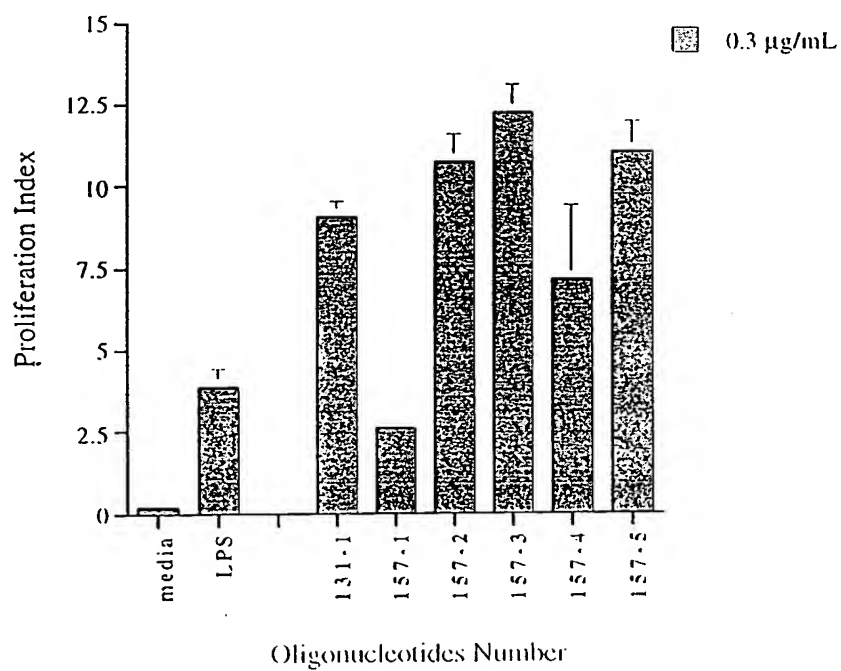


Figure 10 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGACGTTCTCTGT-3' (131-1)
2	5'-CTATCTGXCGTTCTCTGT-3' (157-1)
3	5'-CTATCTXACGTTCTCTGT-3' (157-2)
4	5'-CTAXCTGACGTTCTCTGT-3' (157-3)
5	5'-CTATCTGACGTXCCTGT-3' (157-4)
6	5'-CTATCTGACGTTCCXCTGT-3' (157-5)

**X =**

Amino-Linker

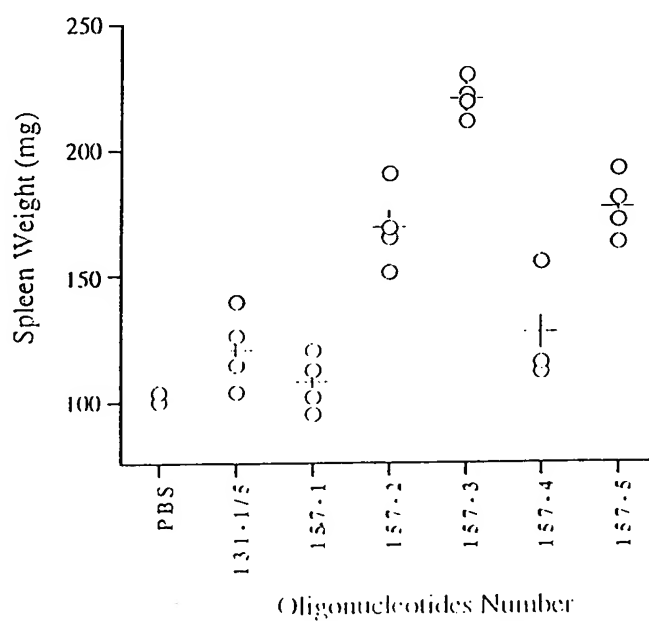
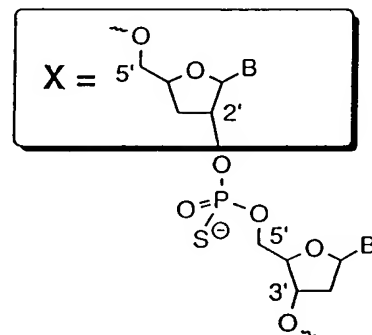


Figure 11 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
159-1	5'-CTATCTGACXTTCTCTGT-3'
159-2	5'-CTATCTGAXGTTCTCTGT-3'
159-3	5'-CTATXTGACGTTCTCTGT-3'
159-4	5'-CTATCTGACGTTCTXTGT-3'
133-1	5'-CCTACTAGCGTTCTCATC-3'
161-1	5'-CCTACTAGCXTTCTCATC-3'
161-2	5'-CCTACTAGXGTTCTCATC-3'
161-3	5'-CCTACTAXCGTTCTCATC-3'
161-4	5'-CCTAXTAGCGTTCTCATC-3'
161-5	5'-CCTACTAGCGTTCTXATC-3'



3'-Deoxynucleoside

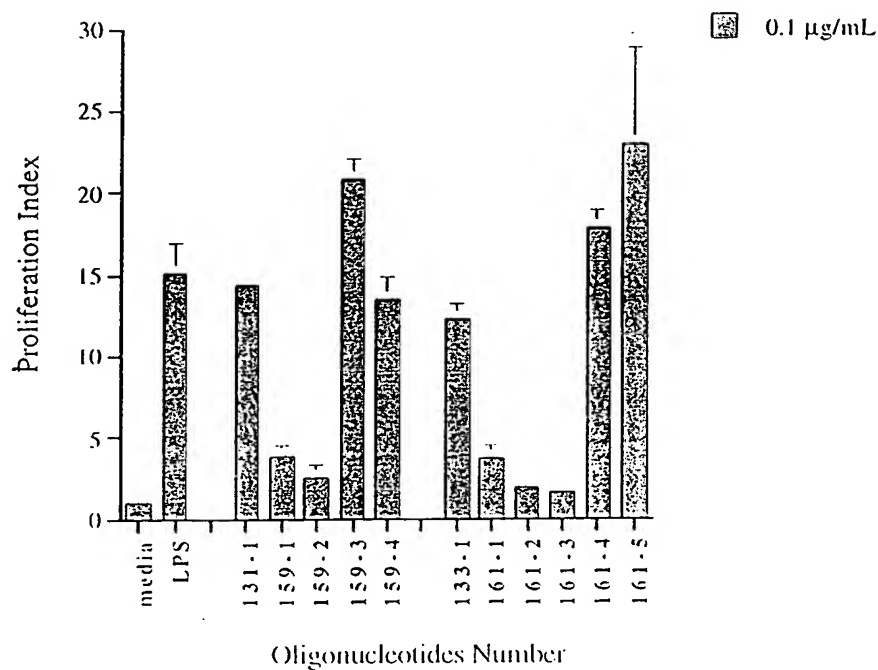
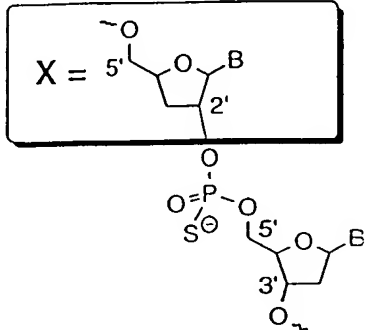


Figure 12 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
159-1	5'-CTATCTGACXTTCTCTGT-3'
159-2	5'-CTATCTGAXGTTCTCTGT-3'
159-3	5'-CTATXTGACGTTCTCTGT-3'
159-4	5'-CTATCTGACGTTCTXTGT-3'
133-1	5'-CCTACTAGCGTTCTCATC-3'
161-1	5'-CCTACTAGCXTTCTCATC-3'
161-2	5'-CCTACTAGXGTTCTCATC-3'
161-3	5'-CCTACTAXCGTTCTCATC-3'
161-4	5'-CCTAXTAGCGTTCTCATC-3'
161-5	5'-CCTACTAGCGTTCTXATC-3'



3'-Deoxynucleoside

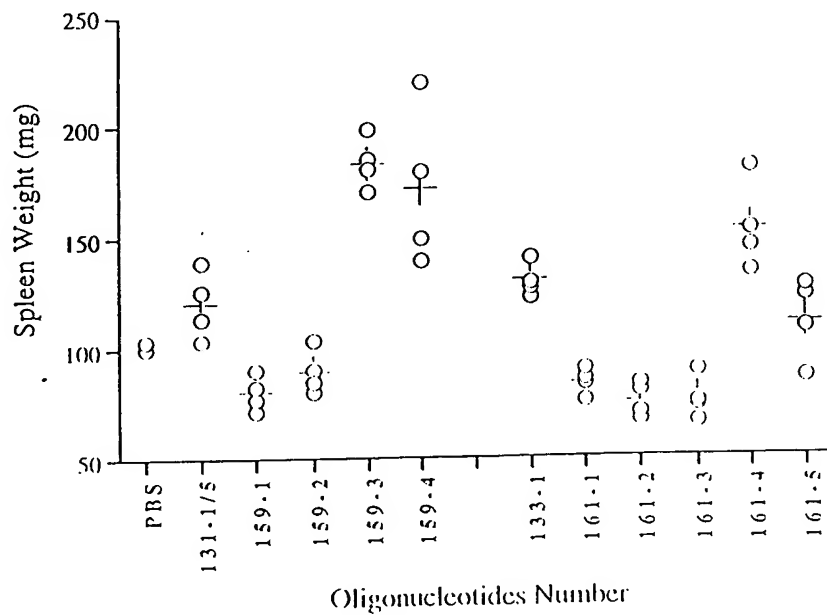


Figure 13 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
167-1	5'-CTATCTGXCGTTCTCTGT-3'
167-2	5'-CTATCTXACGTTCTCTGT-3'
167-3	5'-CTATCXGACGTTCTCTGT-3'
167-4	5'-CTATXTGACGTTCTCTGT-3'
167-5	5'-CTAXCTGACGTTCTCTGT-3'
167-6	5'-CTXXCTGACGTTCTCTGT-3'
167-7	5'-CTATCTGACGXTCTCTGT-3'
167-8	5'-CTATCTGACGTXCTCTGT-3'
167-9	5'-CTATCTGACGTTXTCTGT-3'
167-10	5'-CTATCTGACGTTCTXCTGT-3'
167-11	5'-CTATCTGACGTTCTXTGT-3'
167-12	5'-CTATCTGACGTTCTXXGT-3'

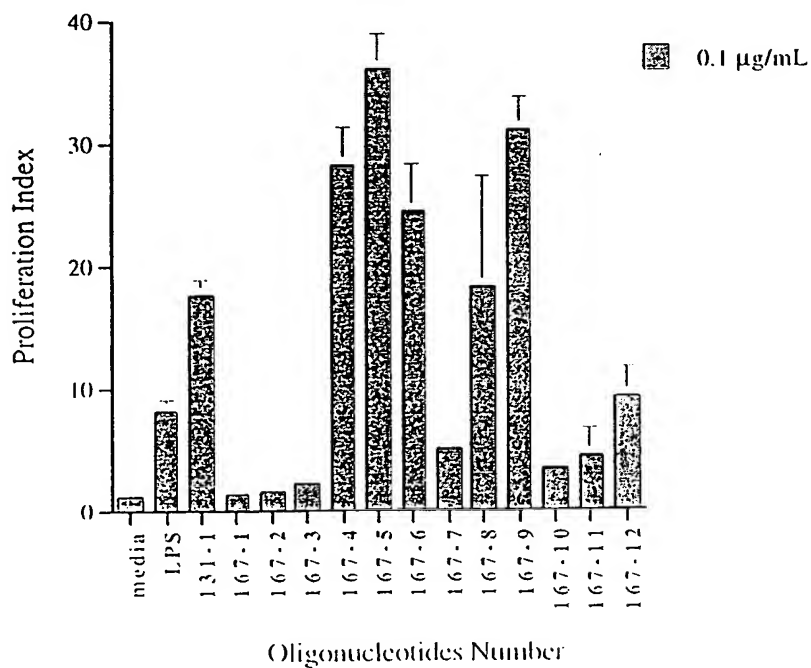
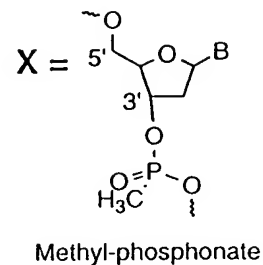


Figure 14 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
167-1	5'-CTATCTGXCGTTCTCTGT-3'
167-2	5'-CTATCTXACGTTCTCTGT-3'
167-3	5'-CTATCXGACGTTCTCTGT-3'
167-4	5'-CTATXTGACGTTCTCTGT-3'
167-5	5'-CTAXCTGACGTTCTCTGT-3'
167-6	5'-CTXXCTGACGTTCTCTGT-3'
167-7	5'-CTATCTGACGXTCTCTGT-3'
167-8	5'-CTATCTGACGTXCTCTGT-3'
167-9	5'-CTATCTGACGTTXTCTGT-3'
167-10	5'-CTATCTGACGTTCTCXGT-3'
167-11	5'-CTATCTGACGTTCTXTGT-3'
167-12	5'-CTATCTGACGTTCTXXGT-3'

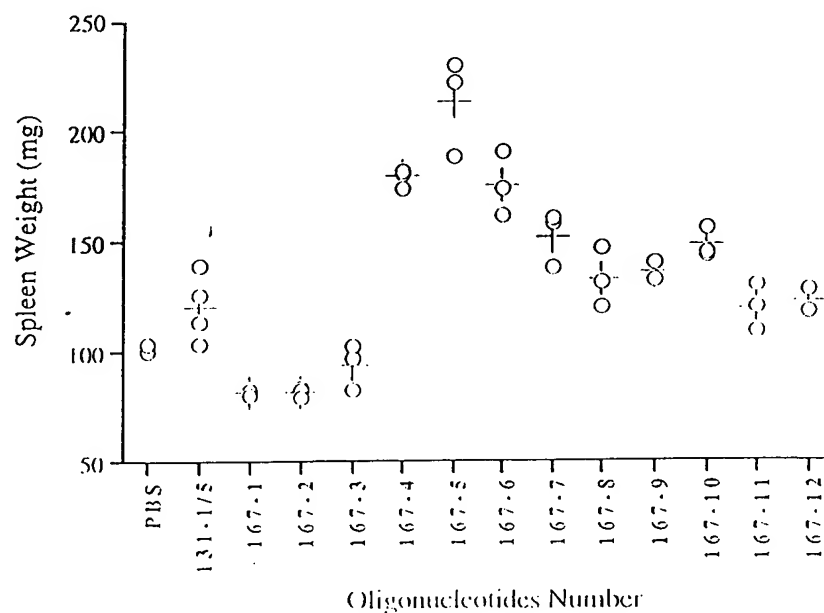
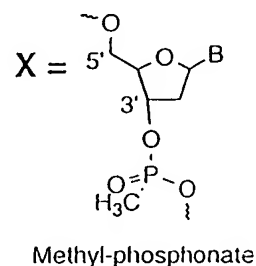
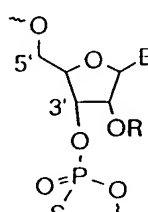


Figure 15 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification	
113-1	5'-TCCATGACGTTCTGATGC-3'	 <p> <math>R_x = 2\text{'-O-Methylribonucleoside}</math>  <math>R_y = 2\text{'-O-Methoxyethylribonucleoside}</math> </p>
23-1	5'-TCCATGXCGTTCCTGATGC-3'	
23-3	5'-TCCAXGACGTTCTGATGC-3'	
29-2	5'-TYYATGACGGTCCTGATGC-3'	

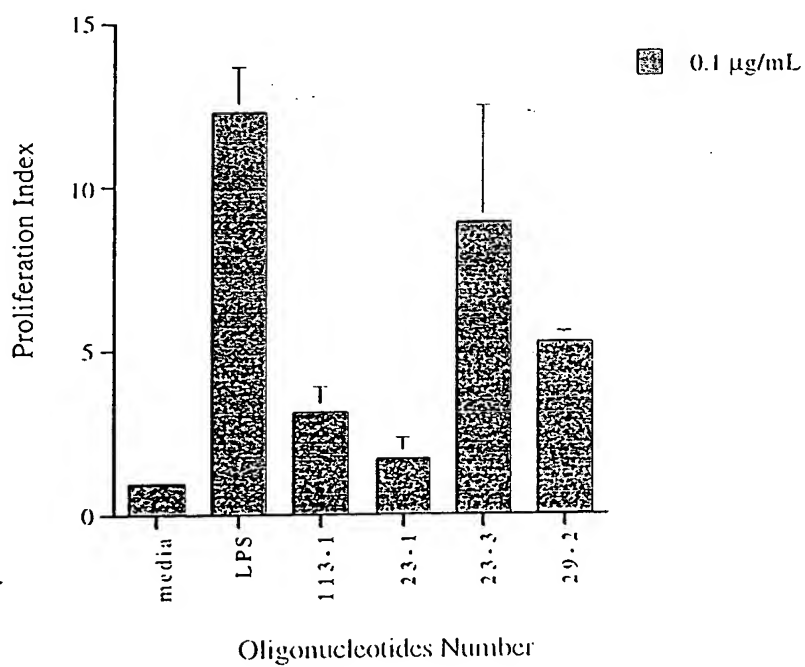
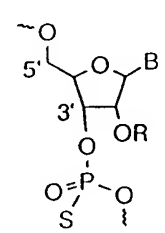




Figure 16 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification	
113-1	5'-TCCATGACGTTTCCTGATGC-3'	
23-1	5'-TCCATGXCGTTTCCTGATGC-3'	
23-3	5'-TCCAXGACGTTTCCTGATGC-3'	
29-2	5'-TYYATGACGGTCCTGATGC-3'	

$R_x = 2'\text{-O-Methylribonucleoside}$   
 $R_y = 2'\text{-O-Methoxyethylribonucleoside}$

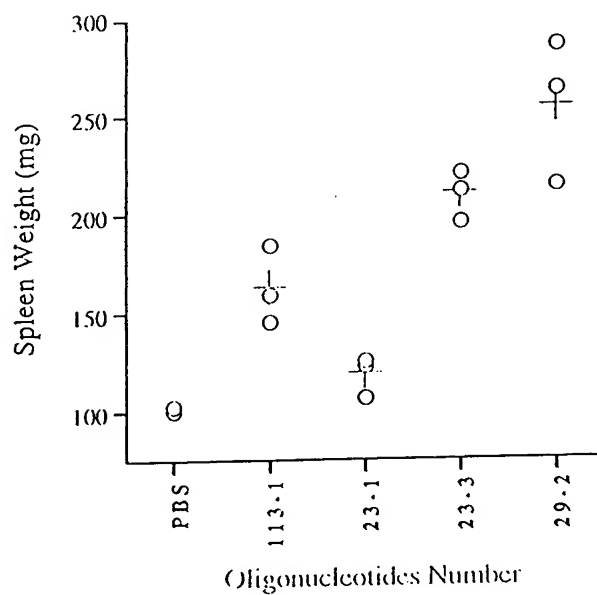
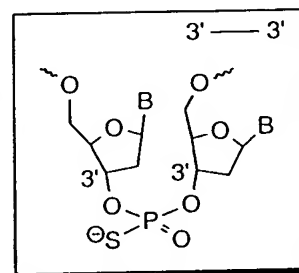
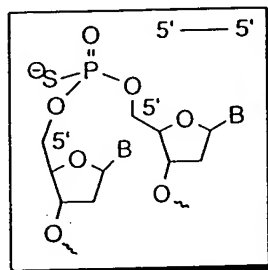
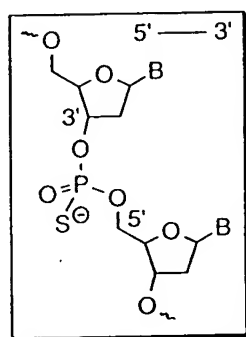


Figure 17 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
1	5'-GAGAACGCTCGACCTT-3'
2	5'-GAGAACGCTCGACCTT-3' — 5'-GAGAACGCTCGACCTT-3'
3	3'-TTCCAGCTCGCAAGAG-5' — 5'-GAGAACGCTCGACCTT-3'
4	5'-GAGAACGCTCGACCTT-3' — 3'-TTCCAGCTCGCAAGAG-5'
5	5'-TCTCCCAGCGTGCGCCAT-3'
6	5'-TCCCAGCGTGCGCCAT-3' — 5'-TCCCAGCGTGCGCCAT-3'
7	3'-TACCGCGTGCGACCCT-5' — 5'-TCCCAGCGTGCGCCAT-3'
8	5'-TCCCAGCGTGCGCCAT-3' — 3'-TACCGCGTGCGACCCT-5'



→ 5'-3'- direction of CpG motif

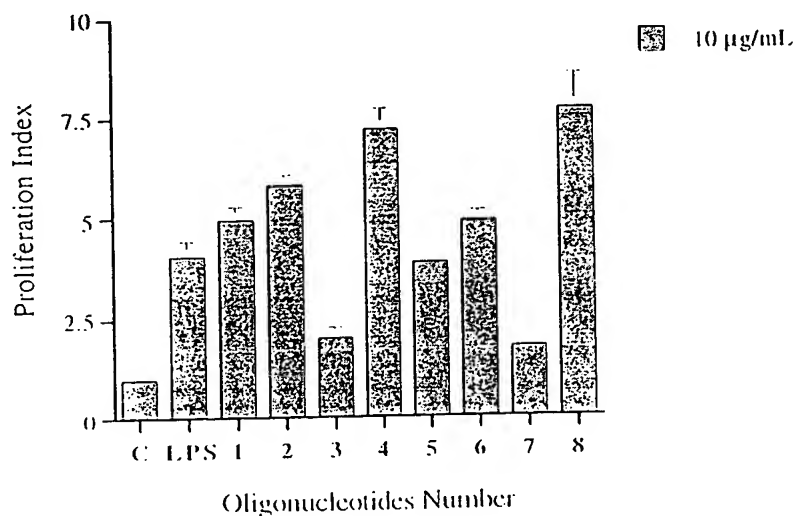


Figure 18 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
175-1	5'-CTATXTGACGTTCTCTGT-3'
175-2	5'-CTATCTGACGTTCTCTGT-3'
175-3	5'-CTAXXTGACGTTCTCTGT-3'
175-4	5'-CTATCTGACGTTCTCTGT-3'
175-5	5'-CTATCTGAXXTCTCTGT-3'
175-6	5'-CTATCTXACGTTCTCTGT-3'
175-7	5'-CTATCTGACGTCTCTGT-3'
175-9	5'-CTATCTGACGTTCTCTGT-3' (all-β-L-DNA/PS)

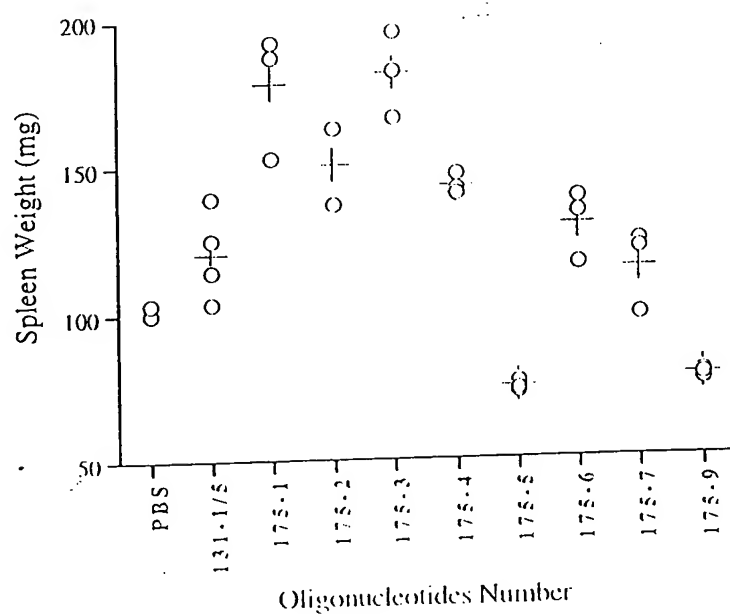
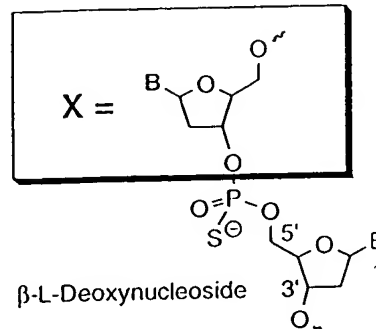


Figure 19 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification	
131-1	5'-CTATCTGACGTTCTCTGT-3'	$X = \begin{array}{c} \sim O \\   \\ 5' - C \\   \quad   \\ 3' - C - O - B \\   \quad   \\ O - P(=S)(O^-) - O - CH_2 - C \equiv CH \end{array}$
173-1	5'-CTATXTGACGTTCTCTGT-3'	
173-2	5'-CTATCTGACGTTCTXTGT-3'	

2'-O-Propargyl-ribonucleoside

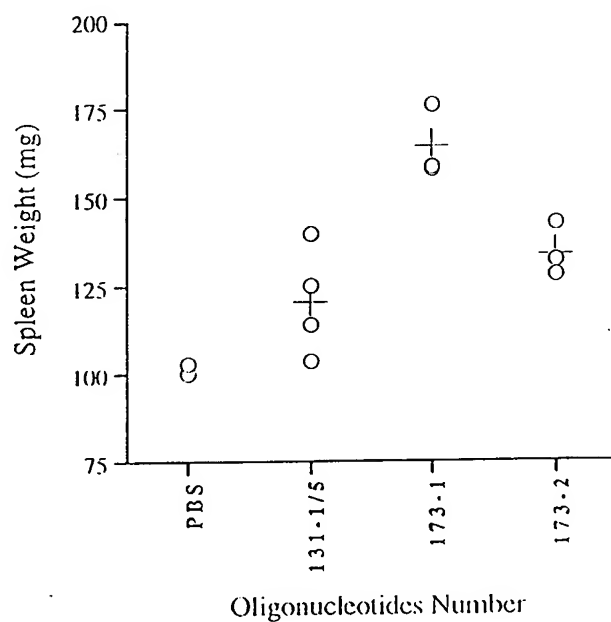


Figure 20 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
133-1	5'-CCTACTAGCGTTCTCATC-3'
143-1	5'-CCTXXTAGCGTTCTCATC-3'
143-2	5'-CCTYYTAGCGTTCTCATC-3'
143-3	5'-CCTZZTAGCGTTCTCATC-3'
143-4	5'-CCTXXTAGCGTVCTCATC-3'
143-5	5'-CCTACTAG <u>G</u> CTTCTCATC-3'

X = 1',2'-Dideoxyribose  
 Y = C3-Linker  
 Z = 3'-OMe  
 V = 2'-OMe

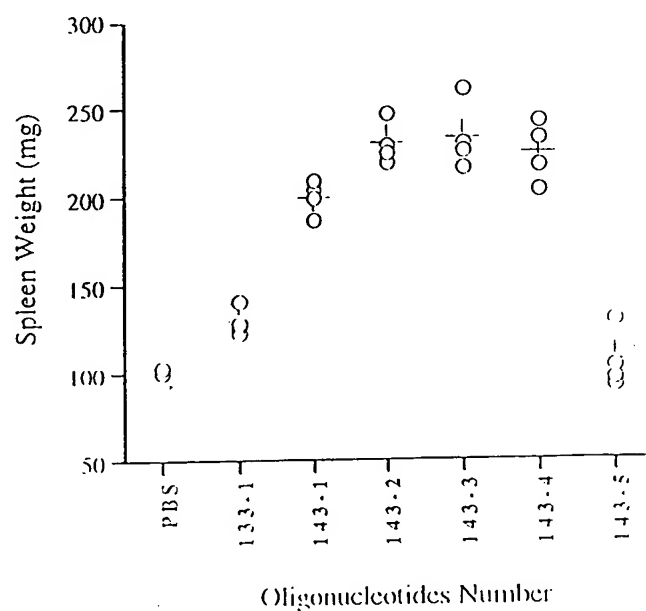


Figure 21 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>CG</u> TTCTCTGT-3' (131-1)
2	5'-CTATCTGAC <u>CG</u> *TTCTCTGT-3' (E 633L)
3	5'-CTATCTGAG*CTTCTCTGT-3' (E 636)
4	5'-TCTCCCAG <u>CG</u> TG <u>CG</u> CCAT-3'
5	5'-TCTCCCAG <u>CG</u> *TG <u>CG</u> *CCAT-3' (E 603)
6	5'-CTATXTGAC <u>CG</u> *TTCTCTGT-3' (E 639L)

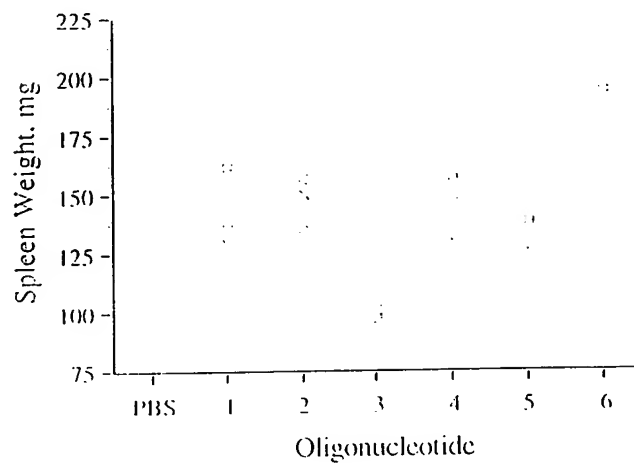
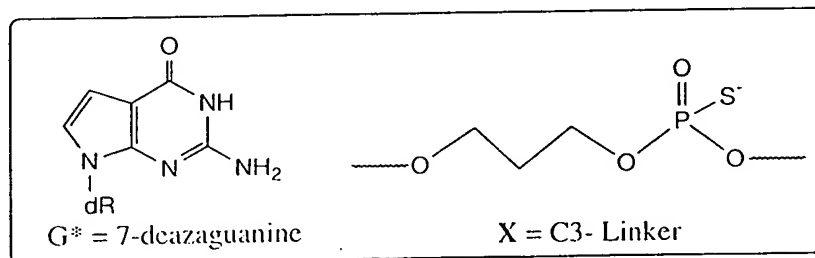
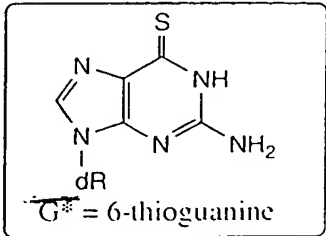


Figure 22 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTCTCTGT-3' (131-1)
2	5'-CTATCTGAC <u>G</u> *TTCTCTGT-3' (E 682)
3	5'-CTATCTGAG* <u>C</u> TTCTCTGT-3' (E 683)



G\* = 6-thioguanine

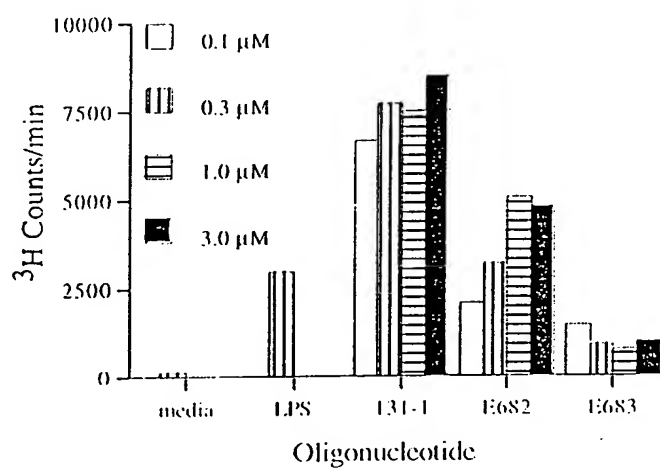


Figure 23 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>CG</u> TTCTCTGT-3'
2	5'-CTATCTGAC* <u>G</u> TTCTCTGT-3'
3	5'-CTATCTGAC <u>CC</u> *TTCTCTGT-3'
4	5'-CTATCTGAC** <u>G</u> TTCTCTGT-3'
5	5'-CTATCTGAC <u>CC</u> **TTCTCTGT-3'

C\* = 5-hydroxy-cytosine    C\*\* = N4-ethyl-cytosine

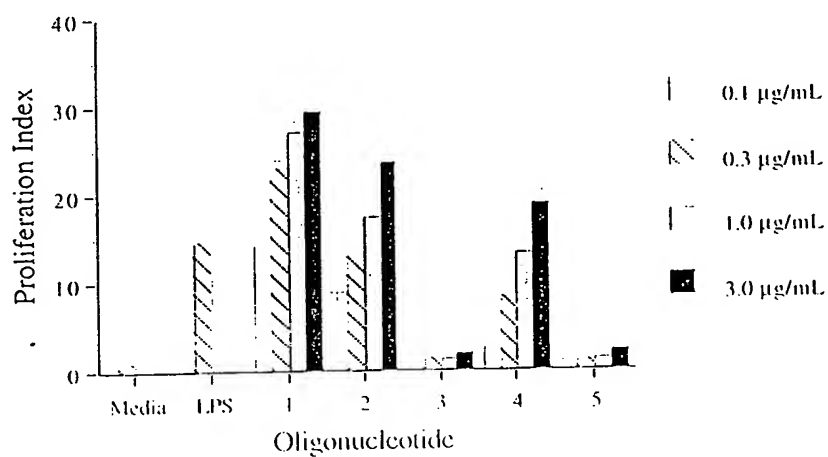
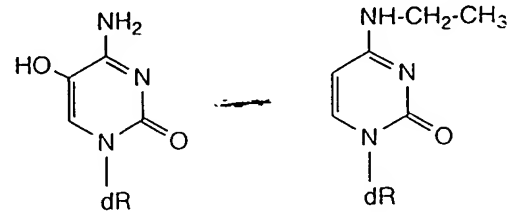




Figure 24 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>CG</u> TTCTCTGT-3'
2	5'-CTATCTGAC* <u>G</u> TTCTCTGT-3'
3	5'-CTATCTGAC <u>C</u> *TTCTCTGT-3'
4	5'-CTATCTGAC** <u>G</u> TTCTCTGT-3'
5	5'-CTATCTGAC <u>C</u> **TTCTCTGT-3'



C\* = 5-hydroxy-cytosine    C\*\* = N4-ethyl-cytosine

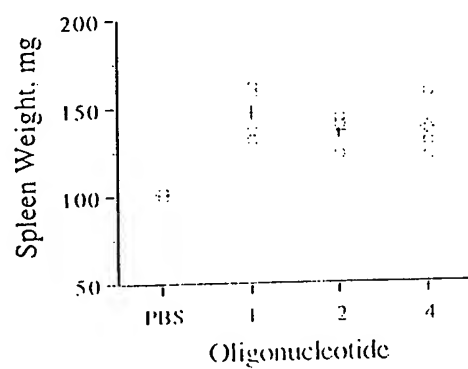


Figure 25 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>CG</u> TTCTCTGT-3'
2	5'-CTATCTGAC <u>G</u> *TTCTCTGT-3'
3	5'-CTATCTGAC <u>CC</u> *TTCTCTGT-3'

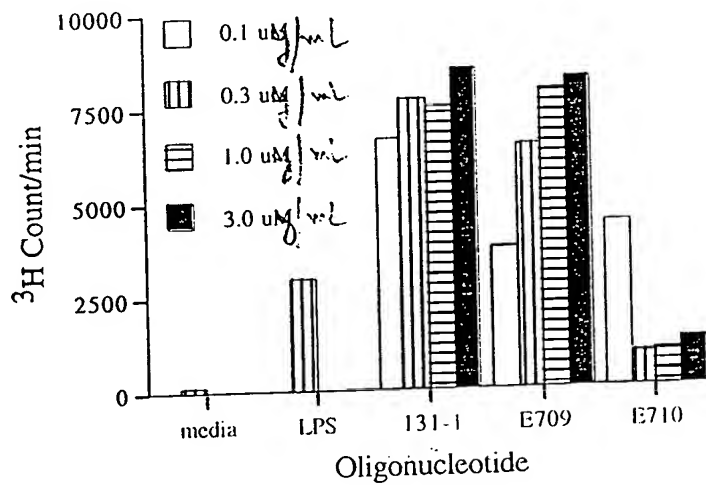
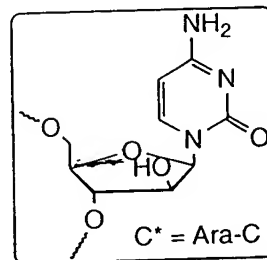


Figure 26 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.      Sequence & Modification

- 1      5'-CTATCTGACCGTTCTCTGT-3' (131-1)
- 2      5'-CTATCTGAC\*GTTCTCTGT-3' (E 647)
- 3      5'-CTATXTGAC\*GTTCTCTGT-3' (E 653)

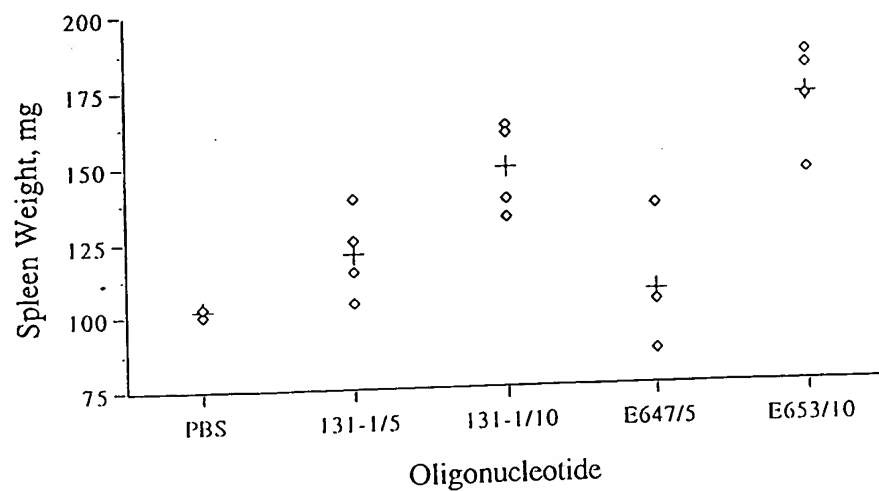
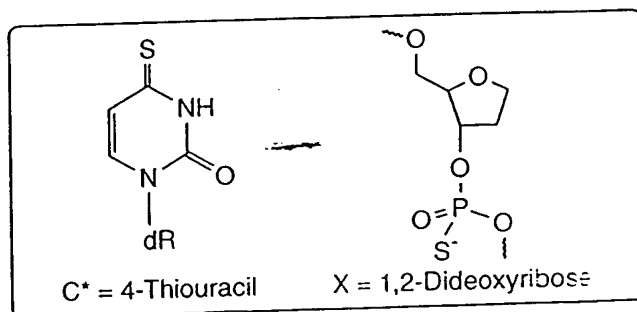


Figure 27

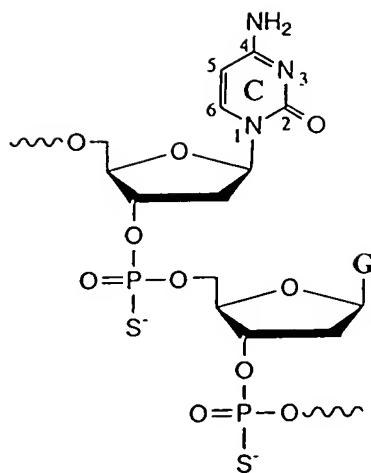


Figure 28

